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Rezumat

Studiile referitor la rolul moleculelor cu masă moleculară medie în practica medicală se efectuează pe larg pentru a estima gravitatea proceselor patologice, a prognoza maladia, precum şi pentru a aprecia eficacitatea metodelor de dezintoxicare extracorporală, ca hemosorbţia, hemodializa, plasmafereza. Autorii, în baza investigaţiilor, au stabilit că în patogenia arsurilor la copii şi a modificărilor multiorganice rolul decisiv îl deţin factorul microbian şi endotoxinele. Pentru aprecierea gradului de intoxicare endogenă, a asocierii complicaţiilor şi concentraţiei substanţelor necrotice e necesar însă de apreciat nivelul peptidelor cu masa moleculară medie.

Summary

Studies regarding the role of medium molecular weight molecules in medical practice are widely used to estimate the severity of pathological processes, predict disease and to assess the efficacy of extracorporeal detoxification methods like hemosorbtion, hemodialysis, plasmapheresis. Authors, based on investigational data, established that in the pathogenesis of burns in children, and the multiorganic changes the main role is played by microbial endotoxins. But to assess the degree of endogenous intoxication, the association of complications the main factor is the concentration of medium molecular weight peptides.

Резюме

Как следует из представленного обзора, исследование показателя уровня средних молекул в практической медицине широко используется для определения степени тяжести патологических процессов и прогнозов заболевания, а также в качестве критерия эффективности методов экстракорпоральной детоксикации – гемабсорбции, гемодиализа, плазмафореза. На основании исследования было установлено, что в патогенезе ожогов у детей и изменениях всех систем основную роль играют микробный фактор и эндотоксины. Но для определения степени эндогенной интоксикации, сопутствующих осложнений и концентрации некротических масс необходимо определить уровень пептидов с средней молекулярной массой.

LIPID PEROXIDATION AND ANTIOXIDANT PROTECTION IN THERMAL BURNS IN CHILDREN

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Introduction

Thermal burns in children have long been burdened with major complications and increased mortality. Various complications are known, but some of the most feared are septic complications.

The problem of preventing sepsis in burns has raised many surgical innovations in how to restore the continuity of the damaged tissue. Until now it can not be asserted the superiority of any of those techniques, as thee benefits are based on a progressive deterioration of function of various organs and systems, which homeostasis can not be maintained without an adequate diagnosis and without a therapeutic intervention. Consequences of those organ and system dysfunction are highly variable regarding the prognosis of the patient with burns.

Today, it is preferred to talk about organ dysfunction - a broad term that expresses a range of functional disturbances, in which the failure of an organ means the stop of its activity (eg, anuria in cases of acute renal failure).

Several endogenous sources generating free radicals were found, as the activation of phagocytes (oxidative burst), as the result of tissue necrosis, and microbial invasion in septic shock and direct activation of xanthine oxidase as a secondary product of arachidonic acid cascade activation.

A more difficult problem is to determine how free radicals are involved in patients with thermal burns. The most studied effect of oxygen derivates radicals is their involvement in oxidative destruction of polyunsaturated fatty acids, a phenomenon known as "lipid peroxidation". Proteins are also subject to oxidative process under the action of O_2, H_2O, NO.

Oxidative modifications of proteins varies depending on the nature of oxidant and the protein studied. Through lipid peroxidation molecular stable products are generated, most important being toxic aldehydes. This creates a basis for dissemination of toxigenic substances of lipid peroxidation. Last reacts with thiol groups of glutathione, cystine, protein, amino groups of some amino acids and inhibit enzymatic activity, having different effects on cells and organs, especially in the growing organism.

Thus, the damage in the primary stage of burns, accompanied with major shock and sepsis focus on microcirculation and medium molecular weight proteins activated to aggregate and adhere to the epithelium, releasing mediators that are able to destroy microvascularization. In the late stages of combustional sepsis and septic shock macrophages are destroyed, capable to secret over 100 different products that play a crucial role in triggering vicious circles leading to cellular-organic damage.

Studies conclude that free radicals, oxygen derivatives are considered very important mediators of production of tissue damage after episodes of ischemia (reperfusion and septic shock).

Fundamental mechanism of free radicals generation in severe burns is the impairment of the blood flow and microcirculation, hypoxia, endogenous intoxication, infection, etc. In the acute phase of the thermal injury on the background of increased vascular permeability and the sequestration of plasma into the interstitial spaces, absolute and relative hypovolemia develops, as well as the centralization of the blood circulation. The last has the adaptive role, supplying adequate blood flow to the priority organs (brain, heart, lungs), but simultaneously leads to regional and peripheral blood circulation disorder. The accentuation of the microcirculation disorder is accompanied by tissue hypoxia, anaerobic glycolysis activation, formation of active forms of oxygen (AFO), which triggers free radical oxidation processes, with subsequent membrane damage and cell death as a consequence. Such oxidative reactions, leading to the formation of toxic metabolites, include the oxidation of lipid products, which in time are neutralized by the body's antioxidant system. An important role in triggering oxidative stress plays the microbial factor. Massive release into the blood stream of the microbial lipopolysacharides lead to the activation of neutrophils and macrophages, formation of active forms of oxygen and its activation [3].

Thus in the pathogenesis of thermal burns an important place have processes induced by free radicals. Tissues under the thermal action are a powerful source of free radicals, triggering a multitude of chain reactions of lipid peroxidation. The intensity of lipid peroxidation correlates with the severity of the patient's condition and depends on the severity of hypoxia, which develops as a result of reduced ventilation and the microcirculation alteration [7, 5]. Lipid peroxidation products are highly toxic compounds and induce the mitochondria's increase in volume, uncoupling the oxidative phosphorylation, inactivation of thiol enzymes involved in respiration and glycolysis, is disturbing the synthesis of adenosine in cells, oxidation of sulfhydryl groups in proteins, damages the DNA, this could slow down or even stop cell division and growth, violating the permeability of biological membranes.

Lysosomal membrane lipid peroxidation promotes the activation of lysosomal hydrolases, proteolytic enzymes [6]. The activation of the enzyme cleavage products, damage cells, with the formation of various toxic substances (molecules with high medium and low molecular weight).

It is confirmed that oxidative stress in thermal trauma are based on the following: blood flow and microcirculation disturbance, hypoxia, endogenous intoxication, microbial spread and AFO hyperproduction, intensification of lipid peroxid oxidation (LPO) and the development of oxidative stress antioxidant insufficiency. The use in severe burns of the antihypoxanth drugs with antioxidant and membrane stabilizing action, which would reduce the pathogenetic reactions [1, 2, 4].

An important issue remains in the role of lipid peroxidation in children aged 0-5 years with thermal burns. A reasoned scientific approach is missing in the evaluation of oxidation of lipid peroxidation in the wound and the influence on these processes of therapeutic remedies for the topical treatment and effective preparations used for the topical treatment of wounds in patients with burns and their consequences.

The research objectives were:

- Assess of the state of oxidation of lipid peroxidation in children with thermal burns, aged 0 to 5 years;
- To determine the dynamic processes of lipid peroxidation in blood and wound depending on lesion stage process in patients with burns.

Materials and methods

The work is performed in the IMSP SCRC "Em.

Cotaga" burns division. There were 100 patients with thermal injury under supervision, aged between 0 and 5 years with 15% to 60% TBSA burns. Among the patients with burns, the burn disease evolved as serious in 52% and as extremely serious in 27%.

All patients admitted in hospital, in complex intensive care, the infuzional therapy against the shock were included. Blood collecting from patients in the six clinical groups studied was performed on the hospital admission (during the combustional shock) and afterwards (during toxemia, septicotoxemia, preoperative, postoperative) and at discharge. For the proper evaluation of results, all the data were processed statistically. In all statistical collections was determined arithmetic mean (M), the arithmetic mean error (m), standard deviation (?). Data evaluation was performed by the software produced by "Microsoft": relational databases 'StatsDirect' and electronic table "Excel-97". Sure difference due to P <0.05.

Results and discussions

Data on blood plasma content of LPO products, the donors and patients with severe thermal trauma are highlighted in Table.

Our findings indicate that at all stages of clinical evolution of the system are set high concentrations of lipid peroxidation and, in particular during septic-toxemia with +18% (P <0.001), postoperatively with +15% (P <0.001) and at discharge with +3% (P <0.001).

We can conclude that free radicals of oxygen in blood are causing toxic damage to all the organs with function deterioration and multiple organ failure development. The severity of the disorders in organs and systems, as well as disease evolution, depends not only on the severity of trauma, but also on the precocity of the complex treatment.

Analyzing the literature it can be concluded that surgery is just a different stage in the treatment and it is necessary to be adapted to each individual case, based on the severity of organ system dysfunction (lung, kidney, gastrointestinal tract etc.), by solving the sepsis.

State system of lipid peroxidation in blood serum of patients with thermal trauma to the six clinical-evolutionary stages

Groups of patients	*Data*					
	hexane phase			*isopropanol phase*		
	early HPL (uc / ml)	*intermediate HPL (uc / ml)*	*late HPL (uc / ml)*	*early HPL (uc / ml)*	*intermediate HPL (uc / ml)*	*late HPL (uc / ml)*
Witness	2.80 ± 0.06 (100%)	1.22 ± 0.04 (100%)	0.47 ± 0.02 (100%)	1.68 ± 0.05 (100%)	0.85 ± 0.03 (100%)	0.44 ± 0.02 (100%)
Admission	3.08 ± 0.06 *** (110%)	1.35 ± 0.06 (111%)	0.42 ± 0.01 * (89%)	1.83 ± 0.11 (109%)	1.04 ± 0.06 ** (122%)	0.44 ± 0.02 (100%)
Toxemia	3.23 ± 0.04 *** (115%)	1.49 ± 0.04 *** (122%)	0.46 ± 0.02 (98%)	1.96 ± 0.07 ** (117%)	1.07 ± 0.04 *** (126%)	0.44 ± 0.02 (100%)
Septico toxemia	3.30 ± 0.07 ***# (118%)	1.56 ± 0.07 ** (128%)	0.45 ± 0.02 (96%)	1.82 ± 0.0 (108%)	0.94 ± 0.04 0 (111%)	0.37 ± 0.02 # ** # 0 (84%)
Preop.	3.21 ± 0.12 ** (115%)	1.47 ± 0.11 (120%)	0.42 ± 0.03 (89%)	1.90 ± 0.14 * (113%)	0.92 ± 0.05 (108%)	0.34 ± 0.02 *** # # 0 (77%)
Postop.	3.23 ± 0.09 *** (115%)	1.56 ± 0.11 ** (128%)	0.56 ± 0.14 (119%)	1.87 ± 0.10 (111%)	1.03 ± 0.08 (121%)	0.39 ± 0.02 (89%)
Discharge	3.20 ± 0.08 *** (114%)	1.58 ± 0.09 *** (130%)	0.57 ± 0.10 (121%)	1.93 ± 0.12 * (115%)	1.08 ± 0.05 § Δ *** (127%)	0.39 ± 0.02 * (89%)

Note: * – Significant difference from the witness group, p <0.05; ** – p <0.01, *** – p <0.001.

- Significant difference compared to admission group, p <0.05, # # p <0.01,

– p <0.001.

0 – significant difference compared to toxemia group, p <0.05; 00 – p <0.01, 000 – p <0.001.

§ – significant difference compared to septicotoxemia group, p <0.05, §§, p <0.01, §§§ – p <0.001.

Δ–statistically significant difference compared to preoperative group, p <0.05, ΔΔ – p <0.01; ΔΔΔ – p <0.001.

$ – Significant difference compared to postoperative group, p <0.05, $ $ – p <0.01, $$$ – p <0.001.

Prognosis of the burn disease is strictly related to providing irrigation of the tissues and the transportation of oxygen and CO2. The elimination of the products of metabolism, resulting in postagresive metabolism, avoiding sodium and water load of vascular bed, installation of pulmonary edema or preedema, intake of energy substances, antioxidants are necessary conditions for the survival.

Without metabolic support in thermal burns, repair or stabilization phase can not be achieved. Problems which make all clinical stages of disease evolution of burned children are to handle better cellular nutrition and link it to various physiological changes.

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Rezumat

Este prezentat un studiu clinic şi biochimic al stării oxidării peroxidice a lipidelor la 100 de pacienţi – copii în vârstă de 0-5 ani cu arsuri termice. Rezultatele studiului ne-au permis să elaborăm un algoritm de tratament diferenţial cu rezultate bune în timp.

Summary

We present a clinical and biochemical study of peroxidative oxidation of lipids in 100 patients, children aged 0-5 years, with thermal burns. Results of this study allowed us to develop an algorithm for differential treatment with good results over time.

Резюме

Представлены клинические и биохимические результаты перекисного окисления липидов у 100 детей, в возрасте от 0 до 5 лет с термическими поражениями. Результаты проведённого исследования позволяют разработать алгоритм дифференциального лечения с положительными результатами.

BARIERA ANTIOXIDANTĂ ÎN ARTRITA JUVENILĂ IDIOPATICĂ

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Introducere

Patogenia AJI este complexă, în studiu permanent. Un loc separat în perpetuarea răspunsului inflamator îl ocupă stresul oxidativ. În cazul AJI, producerea radicalilor liberi ai oxigenului (RLO) depăşeşte capacitatea antioxidantă celulară [5, 7]. În prezent se cunosc antioxidanţi enzimatici şi neenzimatici. Antioxidanţii neenzimatici pot fi hidrosolubili (acţionează în compartimentul hidrofil) şi liposolubili (acţionează în compartimentul hidrofob). De asemenea, se cunosc antioxidanţi endogeni (sintetizaţi de către organism) şi exogeni (prin aport exterior). Sunt antioxidanţi preventivi, care împiedică formarea RLO, şi antioxidanţi care neutralizează RLO existenţi şi asigură eliminarea lor. Prin donarea unui electron RLO, antioxidanţii stopează reacţia în lanţ. Astfel, are loc cu viteză mare recombinarea RLO şi transformarea lor în molecule stabile. Contracararea acţiunilor nocive ale RLO este posibilă datorită prezenţei sistemelor antioxidante endogene.

Se cunosc 4 categorii de molecule cu acţiune antioxidantă: 1) enzime cu acţiune în special la nivel eritrocitar – superoxiddismutaza (SOD), catalaza, glutation-peroxidaza, glutation-reductaza, glutation-S-transferza; 2) macromolecule cu acţiune în special în ser/plasmă – ceruloplasmina, flavonoidele, albumina, transferina; 3) unii hormoni estrogeni, angiotensina, melatonina; 4) alte molecule – tocoferoli, glutation, carotinoide, acid ascorbic, coenzima Q10, acid uric, acid lipoic. Din punct de vedere chimic, un antioxidant este un reductor care reacţionează cu un oxidant pentru a-l neutraliza. Antioxidanţii se găsesc în orice celulă, sunt molecule care protejează organismul de distrugerile provocate la nivel celular de RLO [1].

Aşadar, bariera antioxidantă este un sistem complicat de enzime, elemente şi substanţe care se formează pentru a proteja organismele aerobe împotriva concentraţiilor crescute de oxigen, din care rezultă producerea de RLO distructive.

Scopul studiului este aprecierea rolului protecţiei antioxidante în diferite variante evolutive ale AJI.

Material şi metode

Studiul clinic randomizat a fost efectuat în secţia de reumatologie a ICŞDOSMC în perioada 2008–2010 şi a inclus 150 de copii cu AJI. Diagnosticul de AJI a fost stabilit în conformitate cu clasificarea